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Comparison of lumbar spine metastasis plans involving different stereotactic radiotherapy devices

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ABSTRACT

***Background*:** We compare plans involving two different stereotactic radiotherapy devices: Cyberknife (CK) and Helical Tomotherapy (HTT) and their results on the lumbarvertebra targets. ***Materials and Methods*:** Ten simulation tomographs of the first lumbar vertebra were selected from among the tomographies of patients who had previously undergone SBRT for any reason. In each planning tomography, two separate clinical target volumes (CTV) were drawn at the first lumbar vertebra, we used 2%, 95% and 98% doses of the target volume (D2, D95, D98) in the plan evaluation. The 2% dose of the planning target volume (PTV) was used for comparison with the hot spot; the 95% dose coverage of CTV was used for the target coverage comparison, and the 98% dose of the target volume was used for the dose volume histogram "shoulder" metric definitionTheHomogeneity Index (HI), new Conformity Index (nCI) and Gradient Index (GI) were evaluated for each planning system and target. ***Results*:** In both groups, CTV1 and CTV2, when compared with D95, the coverage for HTT was found statistically significantly higher. D98 was found to be statistically significantly higher with HTT. In both targets, the CKplans were found to have a higher hot area (D2), and inhomogeneous plans were obtained when compared to HTT. The NCI results were similar, and GI was higher with HTT. ***Conclusion*:** In lumbar vertebra stereotactic radiotherapy, more inhomogeneous plans were obtained with Cyberknife than with the Helical Tomotherapy device. A better gradient index was achieved with Cyberknife, while better coverage was achieved on the HTT plan.

INTRODUCTION

Up to 70% of patients with cancers are found to have skeletal involvement, with the vertebral column being the most common location identified in autopsy series [1]. The vertebral column is a frequent site of metastases, and the skeletal system is the most frequent site of metastases after the lung and liver [2–3].

Stereotactic body radiotherapy (SBRT) ablates tumors through the delivery of precise intensive radiation beams, and is associated with minimal complications. SBRT is characterized by, a highly conformal constructed dosimetry, a sharped gradient from high to low dose areas, and a need for accurate patient positioning [4–9]. Spinal SBRT demands the highest accuracy in dose placement, andan extremely rapid dose fall-off between the vertebral body and the spinal cord should be achieved in patients with vertebral metastasis [10–11]. In addition to multi-image guidance, a sophisticated treatment planning system that accurately models highly modulated small-field beams is indispensable for the achievement of high accuracy in radiation delivery, for which an appropriate treatment planning technique should be used. Typically, such plans require keeping the spinal cord at the maximum dose under the relevant dose constraints, and a quick dose fall-off to avoid the epidural area, andit is possible to meet these criteria through the use of different technologies. Similar target coverage properties have been obtained with different levels of homogeneity and treatment durations in a comparison of plan characteristics [3, 12–14, 15], andsome technologies emerge as being more advantageous than others in terms of dose distribution [13, 14, 16].

While evaluating stereotactic radiotherapy plans, the relationship with risky organs should be considered, as well as the shape of the target. Yang [14] and Ma [12] made a comparison of different systems only for thoracic vertebra SBRT, while there has been date to no comparison of SBRT plans specifically for lumbar vertebra with deeper localization and different OARs. Yang [14] reported the VMAT, HT and Cyberknife plans to be similar when dealing with vertebral body-located volumes, although if the volume peduncle is included, the target winding of HTT emerges as an advantage. It has been further stated that for complex targets, thinner fibers and a greater number of bundles are needed [12].

In the present study we compare two different

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SBRT delivery techniques –Cyberknife and Helical Tomotherapy (HTT) – for a lumbar spinal target. Anatomical differences were taken into account in our study through the use of simulation tomographies of 10 different patients. Variables related to tumor extent were eliminated through the use of metastasis-free vertebral images. By choosing the same vertebra, the limitations related to risky organs and depth were standardized, and it was also possible to compare two separate planning systems with complex and relatively simple targets.

MATERIALS AND METHODS

For the study, 10 tomographs that included the first lumbar vertebra and with no metastasis were randomly selectedfrom among the planning tomographiesheld in our clinic's data bank of patients who had previously undergone SBRT for any reason. Ethics committee approval was obtained from Kartal Lütfi Kırdar City Hospital with the number 514,194.24 dated 27.01.2021. All of the tomographies were in the supine position and the section intervals were 1.25 mm. To standardize the variables related to anatomical localization, it was opted to select the same vertebra for all topographiesand the first lumbar vertebra was duly chosen due to the deep localization of the vertebra, spinal cord, bilateral kidney, and liver and gastrointestinal system restrictions as a complicated target. Then, two separate clinical target volumes (CTV) were delineated for two scenariosof tumors localized on the vertebral corpus and the transverse process in the same tomography, following the guidelines of the 2012 Spinal Radiosurgery Consortium [5]. CTV1 included the corpus and one-side transfer process of the first lumbar vertebra, and CTV2 included the corpus, the one-side transferprocess, and a one-side pedicle of the first lumbar vertebra (figure 1). We equalized the right and left lateralization to 1:1, and thetargets were delineated by a single experienced radiation oncologist, and standardized for all cases. To avoid spinal cord fusion errors and spinal cord movement, the thecal sac surrounded by the bone structure was delineated [6]. In the planning tomography, two CTVs delineated for two different scenarios and Organs at Risk (OAR), including the spinal cord, thecal sac, kidneys, aorta, colon and small intestine, were determined. No margin was given to CTV for the planning target volume (PTV).

The prescribed treatment dose was 24 Gy in three fractions, for which Cyberknife and HTT plans were madethat covered more than 90% of the PTV. The planning goals wereto maximize the volume of the PTV that received 100% of the prescribed dose while giving priority to the planning organ at risk volume (PRV) constraints for the spinal cord, and then to other OARs. To exclude the calculated grid volume changes from the evaluation, the near max volume (0.035 cc) was used rather than the max point dose suggested in the International Commission on Radiation Units and Measurements Report 83 [7]. The used spinal cord constrain was dose received 0.1 cc (D 0.1 cc) <18 Gy in three fractions [8]. The maximum dose for target normalized to 100% and must be within PTV. The prescription isodosewas selected as ≥70% and <90% of the maximum dose, andcoverage <90% than the target volume was not accepted [1]. Based on these objectives, SBRT plans were created for 20 targets based on 10 tomographs, to be delivered using Cyberknife (Accuray, Sunnyvale, CA, USA) with a fixed collimator, and HTT (Accuray, Sunnyvale, CA, USA) (figure 2). The Cyberknife plans were drawn up using the Multi-Plan Treatment Planning System (V. 8.5) with sequential optimization. For each plan, two or three fixed collimators were preferred, and the number of beams was kept under 200. Version 5.0 of the Tomotherapy Planning system was used for the HTT plans. The selected jaw dimensions were 1–2.5 cm, and a pitch of 0.287 and a modulation factor ranging from 2.0 to 3.1 were used for optimization.

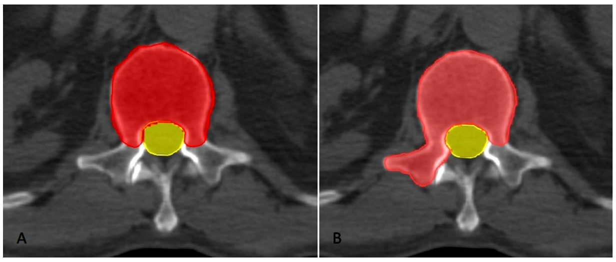

Figure 1. A. CTV1 included the corpus and one-side transfer process of the first lumbar vertebra, B CTV2 included the corpus, the one-side transfer process, and a one-side pedicle of the first lumbar vertebra.

D2, D95 and D98 were determined for a target dose-volume evaluation. For the dose-volume histogram "shoulder" metric definition, the dose that covered 98% of the volume was used for comparison purposes, and the dose that covered 2% was used for comparison with the maximum dose. The dose covering 95% of CTV was used as the target coverage. The Homogeneity Index (HI) was used to determine the dose homogeneity within the target, and the New Conformity Index (nCI) was used for the target dose coverage. The gradient index (GI) was used to evaluate how sharply the dose decreased (table 1).

IBM SPSS statistics (Version 21.0. Armonk, NY: IBM Corp.) was used for the statistical analysis. Data were expressed as mean±standard deviation. The dosimetric characteristics of the techniques were analyzed using a Related-Samples Wilcoxon Signed Rank Test. Values of $p < 0.05$ were considered statistically significant.

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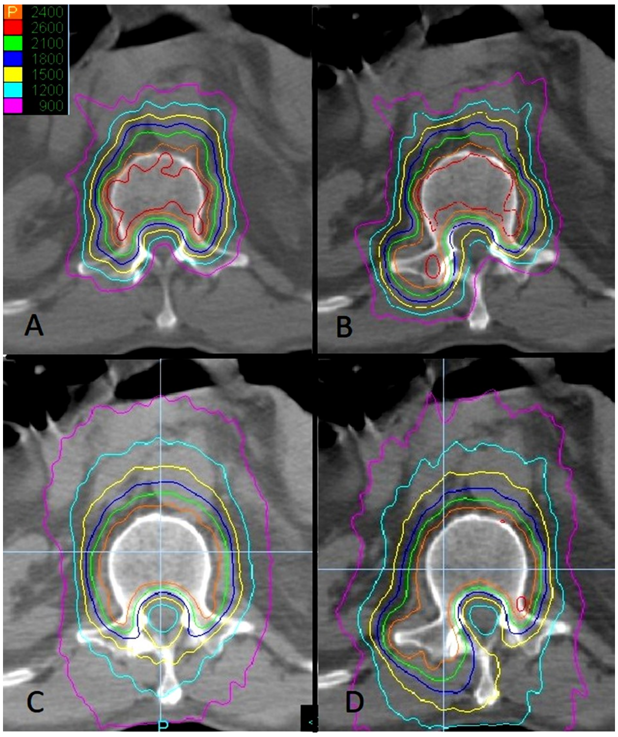

Table 1. Indexes used in the study.

Homogeneity Index	HI: Max / PD Max = maximum dose within target volume, PD = prescribed dose Normal 1.0-2.0
New Conformity Index	nCI = (TV x PIV) / (TVPIV)2 TVPIV = Target Volume covered by Prescription Isodose Volume TV = Target Volume, PIV = Prescription Isodose Volume Normal 1.0-2.0
Gradient Index	GI = PIV_{half} / PIV PIV_{half} = Prescription isodose volume, at half the prescription isodose PIV = Prescription isodose volume

RESULTS

The mean PTV volume was 42.46 cc (min: 33.68–max: 57.41 SD: 7.79) for the vertebral corpus contour set, and 46.40 cc (min: 37.27–max: 62.21 SD: 8.49) forthe vertebral corpus and pedicle. The maximum dose and D0.1 cc value for the spinal cord were similar, and there were no statistical differences identified between all plan sets. The spinal cord dose and D95, D2, D98, HI andnCI values are presented in table 2 for both PTV groups, table 3 for the vertebral corpus PTV and table 4 for the vertebra corpus with pedicle PTV. The D95 value for the target was statistically higher in the HTT plans for both the vertebral corpus and the vertebral corpus + pedicle groups. The D2 value for target was higher, and the D98 value for the target was lower in the Cyberknife plans for the vertebral corpus and vertebral corpus with pedicle targets (tables 2, 3, and 4). In both the vertebral corpus and vertebral corpus + pedicle targets, more homogeneous plans were obtained with HTT than with Cyberknife. The NCI values were similar in both contour sets when analyzed together and separately. The gradient index was higher with HTT across the entire group, while in contrast, no significance was observed in the evaluation of the corpus and corpus + pedicle PTV groups.

Table 2. Index values of corpus and corpus + pedicle for both machines.

	Cyber-Knife		Helical Tomotheraphy		
	Min-Max	Mean±SD[a]	Min-Max	Mean±SD	P[b]
Spine D_{max} (cGy)[c]	1718-1902	1822±7.22	1766-1907	1835±34.38	0.247
Spine $D_{0.1\,cc}$(cGy)[d]	1659-1801	1774±33.60	1702-1798	1763±27.81	0.351
D_2(cGy)[e]	2785-2999	2876±55.27	2486-2739	2573±7094	0.000
D95 (cGy)[f]	1857-2168	2012±77.31	1996-2206	2125±5476	0.000
D98 (cGy)[g]	1735-1995	1851±61.69	1761-2037	1923±62.07	0.000
HI[h]	1.19-1.28	1.22±0.02	1.06-1.19	1.11±0.03	0.000
NCI[i]	1.36-1.70	1.56±0.09	1.38-1.89	1.59±0.13	0.304
GI[j]	3.67-5.28	4.33±0.41	3.63-5.81	4.67±068	0.004

Table 3. Index values of the corpus for both machines.

Corpus	CyberKnife		Thomotherapy		
	Min-Max	Mean±S.D.[a]	Min-Max	Mean ± S.D.	P[b]
Spine D_{max}[c]	1718-1855	1816.1±39.22	1802-1907	1843.4±33.87	0.593
Spine D0.1[d]	1659-1797	1765.4±39.06	1723-1798	1770.9±25.98	0.572
D95 (cGy)[e]	1959-2168	2061.7±63.88	2100-2206	2153.7±33.51	0.003
D2 (cGy)[f]	2785-2967	2882.9±57.01	2486-642	2560.1±55.44	0.000
D98 (cGy)[g]	1807-1995	1886.1±58.35	1877-2037	1958.7±43.38	0.016
HI[h]	1.19-1.27	1.23±0.02	1.06-1.17	1.11±0.03	0.000
NCI[i]	1.36-1.58	1.49±0.07	1.38-1.69	1.57±0.11	0.081
GI[j]	3.67-4.61	4.07±0.31	3.63-4.73	4.29±0.43	0.199

Table 3. Index values of the corpus for both machines.

Corpus+pedicle	CyberKnife		TomoTherapy		
	Min-Max	Mean ± SD[a]	Min-Max	Mean ± SD	P[b]
D_{max} (cGy)[c]	1755-1902	1828.2±36.13	1766-1894	1826.1±34.38	0.871
$D_{0.1}$ (cGy)[d]	1729-1801	1782.3±26.44	1702-1794	1756.0±28.92	0.113
D95 (cGy)[e]	1857-2019	1961.8±54.72	1996-2169	2096.2±58.06	0.000
D2 (cGy)[f]	2791-2999	2868.6±55.54	2500-2739	2585.2±84.86	0.000
D98 (cGy)[g]	1735-1874	1816.5±44.04	1761-1964	1887.9±58.88	0.010
HI[h]	1.19-1.28	1.22±0.02	1.06-1.19	1.12±0.04	0.000
NCI[i]	1.46-1.70	1.63±0.06	1.42 -.89	1.61±0.15	0.705
GI[j]	4.12-5.28	4.59±0.33	3.70-5.81	5.05±0.69	0.096

a. SD: Standard Deviation,
b. Related-Samples Wilcoxon Signed Rank Test
c. Spinal cord D max: The dose of the spine 0.035 cc volume
d. Spinal cord D 0.1cc: The dose of the spine 0.1 cc volume
e. D2: Dose of 2% of the target volume
f. D95: Dose of 95% of the target volume
g. D98: Dose of 98% of the target volume
h. HI: Homogeneity index
i. NCI: New Conformity Index
j. GI: Gradient Index

DISCUSSION

Today, the use of SBRT is increasing exponentially in cases of spinal metastases. VertebraSBRT requires a complex treatment plan due to its association with the spinal cord and other risky organs, and the Plan requirements can be met by many technologies [13, 15]. When different technologies are available, it is important to choose the most appropriate system for the patient and the target outcomes.

For cyberknife, which has the advantage of allowing the real-time monitoring of patients with

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spinal metastases, the treatment time is longer, and the treatment plans are more inhomogeneous than others systems [3,12,15]. When compared to VMAT, which has more monitor units (MU), better D2, D5, D95, conformity index and gradient index values are achieved, as reported by Aljabab *et al.* [3]. Better conformity was achieved, however, with the HTT plan for spine metastases when compared to the volumetric arc plan, and a higher 95% target volume coverage was obtained [3].

As expected, in a comparison of the Cyberknife and HTT systems, the treatment time with Cyberknife is longer. In dose planning, the primary priority is considered to be spinal cord limitation, and Aljabab *et al.* achieved similar target coverage and conformity with Cyberknife and HTT, although the authors reported a higher HI with Cyberknife [3]. Similarly, better coverage (higher D95) with HTT and more homogeneous plans were achieved with lower cold-hot areas in the present study, that we determined compliance with spinal cord limitation as a primary goal.

Yang *et al.* found that the HTT plans had significantly better conformity to the target than the Cyberknife plans, and while no significant differences were observed related to the homogeneity of the target, the authors reported inconsistent dosimetric advantages of the two plans for individual OARs. Better dose conformity, a similar dose homogeneity and a poorer dose gradient were obtained with HTT when compared with Cyberknife. An overall plan analysis using the CI confirmed the dosimetric advantage of HTT, although not all indices revealed a better outcome for HTT [14].

When evaluating planning systems in stereotactic radiotherapy, the target volume, and shape and its relationship with risky organs should obviously be taken into consideration. It has been shown that a better performance can be achieved with specific modalities for different target shapes and locations [13–14, 16]. Studies evaluating the location of the vertebra, where the SBRT will be applied, the location of the tumor and the features of the planning system are few in number. With different contour sets of thoracic and lumbar vertebrae in the phantom, Gallo [15] reported the lowest spinal cord doses and the fastest dose reduction to be achieved with Cyberknife (Accuray, Sunnyvale, CA, USA) rather than with tomotherapy (Accuray Sunnyvale, CA, USA), Vero (BrainLAB, Feldkirchen, Germany) and Mitsubishi Heavy Industries (Tokyo, Japan), and Varian TrueBeam and RapidArc (Varian Medical Systems, Palo Alto, CA, USA). Yang et al. reported the SBRT experiences delivered using Cyberknife, Rapid arc, IMRT and HTT systems in thoracic vertebral volumes [14], and found Cyberknife to have the most dose heterogeneity and the longest treatment time, while IMRT had poorer coverage than Cyberknife, RA and HTT for both body type lesions and body with pedicle lesions. The authors reported that VMAT, HTT and Cyberknifeplans were similar in vertebral body volumes, But reported that greater intended coverage was achieved with HTT when the pedicle was included in the volume [14].The lumbar vertebrae have different features to thoracic vertebras due to the deep placement and their proximity to OARs. In our study, with the HTT, a more homogeneous plan was developed for the corpus and corpus pedicle plan for the deeply located lumbar vertebra than in the Cyberknife plan, and better coverage was achieved.

Nalichowski *et al.* [13] compared the Flattening Filter Free RapidArc, Tomotherapy, Cyberknife and Vero systems for four different target lesions located in both the thoracic and lumbar spine regionsusing an SBRT phantom. Cyberknife achieved the lowest spinal cord doses and the lowest gradient indexoverall, and reported the use of Cyberknifeto be advantageous for small volumes. In our study, a better gradient index was obtained with Cyberknifethan with tomotherapy.

The retrospective nature, the small sample size and the different dose calculation techniquesapplied can be considered limitations of the present study.

CONCLUSION

For stereotactic radiotherapy of the lumbar vertebra, both techniques are suitable in terms of proper dose distribution and spinal cord protection, andboth technologieshave features that offer similar advantages and disadvantages in lumbar vertebra SBRT plans for corpus only and corpus + pedicle transverse processes. Although more homogeneous plans and better coverage were obtained with HTT, there were no statistical differences in the maximum dose or D0.1 cc values for the spinal cord between the Cyberknife and HTT plans. That said, the gradient index was found to be higher with HTT than with Cyberknife.

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Authors Contribution: (N.I) and (E.A) designed the study, CTV contouring done by NI and radiotherapy plans done by E.A . G.Y analyzed data.. All authors discussed the results and wrote the manuscript. AÖ revised the manuscript.

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